UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,069	04/11/2005	Yohko Akiyama	08279.1209USWO	2373

52835 7590 06/05/2009

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
P.O. BOX 2902
MINNEAPOLIS, MN 55402-0902

EXAMINER	
SHTERENGARTS, SAMANTHA L	
ART UNIT	PAPER NUMBER
1626	
MAIL DATE	DELIVERY MODE
06/05/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,069	AKIYAMA ET AL.	
	Examiner	Art Unit	
	Samantha L. Shterengarts	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *amendments filed 12 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *1-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-49 are currently pending in the instant application. Claims 1-40 remain withdrawn for being drawn to a non-elected invention.

Response to Amendment

2. Amendments filed November 12, 2008 are acknowledged.

3. All rejections not explicitly maintained herein are withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 41 and 43-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beckert et al. (WO 02/060415) in view of the teachings of Kelm et al. (US 5,656,290). Hereinafter, US 2003/0152627 will be referred to as an English equivalent translation.

With respect to claim 41,43 and 47, Beckert et al. discloses a capsule comprising granules (pellets) having core particles containing lansoprazole (page 4, column 1, lines 12-13) and a pH-dependently soluble release-controlled coating-layer made of methyl methacrylate-methacrylic acid copolymer where the polymeric substance is soluble at a pH of 6.8 [0018], [0046] [0049], [0053], and granules (pellets) comprising core particles containing lansoprazole and an enteric coating that is dissolved, thereby releasing the active ingredient in the pH range above about 5.5 [0019], [0035]. Beckert et al. fails to expressly disclose the exact pH range being between 5.5 and 6.0. Kelm et al. teaches it is well known in the art that the pH is different in various parts of the gastrointestinal system and to utilize different coatings depending on the location of the active ingredient to be released (col. 10, lines 6-16, 47- 60). Therefore it would have been obvious to one of ordinary skill in the art to adjust the pH range depending on the location of the drug to be released. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or working ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

With respect to claims 44 and 45, the modified Beckert et al. discloses the active ingredient (lansoprazole) can be optically active isomers and racemates or mixtures of diastereoisomers [0054].

With respect to claim 46, the modified Beckert et al. discloses the inclusion of a stabilizer [0104], however fails to expressly disclose the stabilizers being a basic inorganic salt. However, it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice. In re Leshin, 125 USPQ 416.

With respect to claim 48, the modified Beckert et al. discloses the pH- dependently soluble release-controlled coating-layer contains a mixture of two or more kinds of methyl methacrylate-methacrylic copolymers that have different release properties [0038], [0047]-[0050].

Applicant's representative writes the following:

Claims 41 and 43-48 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Beckert et al. (International Patent Application Publication No. WO 02/060415) in view of Kelm et al. (U.S. Patent No. 5,656,290). Applicants respectfully traverse this rejection.

Beckert merely discloses lansoprazole in a long list of candidates of active ingredients for a formulation (see para. [0053] at pages 3-4) and fails to disclose any example that includes lansoprazole or compound (I'). In addition, Beckert discloses a capsule formulation including pellet A and pellet B (see paras. [0018]-[0019] at pages 1-2). However, the formulation of Beckert is intended to provide a continuous sustained release in the entire intestinal region (see para. [001] at page 1). A polymer coating used by Beckert in examples to form pellets A and B is EUDRAGIT®, which is water-insoluble and is used to control release in gastro-intestinal tract (see paras. [0031]-[0032] at page 2 and [0048]-[0049] at page 3 and a copy of catalog of EUDRAGIT® attached hereto). Thus, pellet A receives an outer polymer coating and dissolves slowly at pH 6.8 such as 40-70 % for 2 hours and 60-100 % for 4 hours (see paras. [0001] and [0012] at page 1 and [0024] at page 2) as Beckert designs. Pellet B may receive one polymer coating and dissolves slowly such as at pH 6.8, 10 % or less for 2 hours and 20 % or less for 4 hours, and at pH7.2 about 40-60 % for 3 hours (see para. [0046] at page 3). Accordingly, both pellets of Beckert slowly dissolve at pH 6.8-7.2, and Beckert fails to disclose a pellet that dissolves and releases the active ingredient at pH 5.0-6.0 as claim 41 requires. By having composition (ii) dissolving at pH 5.0-6.0 and composition (i) that includes the polymeric substance for controlled release at higher pH 6.0-7.5, the capsule formulation of claim 41 releases the active ingredient rapidly from composition (ii) at the pH of the small intestine, which enhances a blood level at an earlier stage after administration and initiates efficacy of the active ingredient at the earlier stage. Then, the active ingredient that is released from composition (i) later at higher pH 6.0-7.5 maintains the blood level and the efficacy (see page 113, lines 10-22 and page 114, line 23 – page 115, line 10 of the specification). Such a two-step release pattern composition is different from the pattern contemplated by the reference. Accordingly, claim 41 is distinguished from Beckert.

Kelm discloses that pH is different in various parts of the gastrointestinal system (see coln. 10, lines 11-16). Kelm disclose a formulation that delays a release of bisacodyl until the formulation has reached a portion of the colon where pH is greater than 7 (see coln. 10, lines 32-37). The formulation of Kelm includes an outer coating that prevents release of the active ingredient until the formulation reaches a target organ such as colon and dissolves at pH 6.8-7.2 and an inner coating that dissolves at pH 5-6.3 (see coln. 10, lines 42-50). This formulation is basically the same as pellet A of Beckert (see paras. [0024] and [0035] at page 2), and Kelm fails to disclose two compositions, each of which includes an active ingredient. In addition, Kelm discloses only use of bisacodyl. Therefore, Kelm discloses no more than pellet A of Beckert and does not remedy the deficiencies of Beckert.

Response to Arguments

Applicant's representative first asserts that Beckert merely discloses lansoprazole in a long list of candidates of active ingredients for a formulation and fails to disclose any example that includes lansoprazole or compound (I). It is correct that in ¶ [0053] lansoprazole is taught in a list, and not in a working example; however, a reference is not limited to its working examples, but must be evaluated for what it teaches those of ordinary skill in the art. In re Boe, 335 F.2d 961, 148 USPQ 507 (CCPA 1966). In re Chapman, 357 F.2d 418, 148 USPQ 711 (CCPA 1966). One of ordinary skill in the art, based on the list of active ingredients in ¶ [0053], would be motivated to use lansoprazole in the capsule formulation.

Next, applicant's representative asserts that both pellets of Beckert slowly dissolve at pH 6.8-7.2, and Beckert fails to disclose a pellet that dissolves and releases the active ingredient at pH 5.0-6.0 as claim 41 requires. Examiner would like to point to the rejection to address this issue. The following is an excerpt from the original rejection: "pH-dependently soluble release-controlled coating-layer made of methyl methacrylate-methacrylic acid copolymer where the polymeric substance is soluble at a pH of 6.8 [0018], [0046] [0049], [0053], and granules (pellets) comprising core particles containing lansoprazole and an enteric coating that is dissolved, thereby releasing the active ingredient in the pH range above about 5.5 [0019], [0035]." Beckert et al. teaches, in ¶ [0019], "comprises at least two forms of pellets, A and B, which comprise an active pharmaceutical ingredient in the core, but have different polymer coatings which determine the release of the active ingredient at different pH values. In vitro, the USP release test results a pH 6.8 and at pH 7.2 in combined profiles which are between the individual release curves for the two pellet forms A and B. In vivo, the release profile of pellet form A predominates in the small intestine, and release of the active ingredient from pellet form

B starts while in the large intestinal region." It is evident in this paragraph that, as instantly claimed, Beckert discloses the active ingredient soluble in a pH range of 6.0 to 7.5 (both 6.8 and 7.2). In ¶ [0035], Beckert discusses that the outer polymer coating (of either Pellet A or B) rapidly dissolves only above about pH 5.5. This prevents release of the active ingredient in the stomach (which is the same function of the dual release pattern as claimed). Furthermore, Beckert discusses the different pH values at which the active ingredient is released in [0019] as detailed above. Therefore, the release of the active ingredient at two different pH ranges is taught by Beckert.

Finally, Applicant's representative writes that Kelm does not cure the deficiencies of Beckert et al. because it is basically the same as pellet A and fails to disclose two compositions. This is a correct assertion; however, Kelm et al. was not relied on to disclose both compositions. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Kelm et al. is specifically relied upon to show that is well known in the art that the pH is different in various parts of the gastrointestinal system and to utilize different coatings depending on the location of the active ingredient to be released (original rejection). Kelm is relied upon to cure the deficiency that while Beckert does disclose the active ingredient being released at a pH above 5.5, it does not disclose the exact pH range being between 5.5 and 6.0. It would have been obvious to one of ordinary skill in the art to adjust the pH range depending on the location of the drug to be released, as taught by the modified Beckert in view of Kelm et al.

In order to overcome this final rejection, a showing of unexpected results is necessary. If applicant intends to rely on unexpected or unforeseen results, attention is invited to MPEP 716. Absent clear, convincing, side-by-side date demonstrating unobviousness vis-à-vis the prior art commensurate with the scope of protection sought, the claims are considered prima facie obvious.

Maintained Rejections

Claim Rejections - 35 USC § 103

5. Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Beckert et al. in view of the teachings of Kelm et al. and further in view of Karehill et al. (WO 99/32091).

With respect to claim 42, the modified Beckert et al. addresses all the limitations of claim 41, however fails to expressly disclose the pH-dependently soluble release- controlled coating-layer formed on an intermediate layer that is formed on the core particle. Karehill et al. discloses a tablet or pellets comprising a separating layer (intermediate layer) formed on a core particle containing an active ingredient (pg. 6, lines 1-6). It would have been obvious to one of ordinary skill in the art to include an intermediate layer in order to improve the chemical stability of the active ingredient and/or the properties of the dosage form (pg. 17, lines 15-18).

6. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Beckert et al. in view of the teachings of Kelm et al. and further in view of Yamamoto et al. (US 5,264,223)

With respect to claim 49, the modified Beckert et al. addresses all the limitations of claim 41, however fails to expressly disclose the inclusion of a gel-forming polymer. Yamamoto et al. discloses a hard capsule comprising a gel-forming polymer (abstract). It would have been obvious to one of ordinary skill in the art to utilize a gel-forming polymer in order to provide a hard capsule with increased prevention of capsule film cracking for the predictable result of prevention of the deterioration of active ingredients within the capsule (col. 2, lines 25-34).

Response to Arguments

There are no arguments directly related to dependent claims 42-49.

Conclusion

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samantha Shterengarts whose telephone number is (571)270-5316. The examiner can normally be reached on Monday thru Thursday 9-6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

/Samantha L. Shterengarts/
Examiner, Art Unit 1626

/Kamal A Saeed/
Primary Examiner, Art Unit 1626